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Effect of preoperative oral antibiotics in combination with mechanical bowel preparation on inflammatory response and short-term outcomes following left-sided colonic and rectal resections

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Golder *et al.*'s propensity-matched retrospective observational study found the addition of preoperative oral antibiotics and mechanical bowel preparation to prophylactic intravenous antibiotics was associated with reduced postoperative complications and severity of systemic inflammatory response[1]. We believe several statistical issues may have led to the treatment effect being overstated.

First, more patients in the control group had malignant disease; this can lead to a heightened inflammatory state. The *P* values that would have made this obvious were removed between *Table 1* and *Table 2*. Second, the historical nature of the control group, with unmeasured aspects of treatments likely to improve over time, will lead to improved outcomes in the treatment group. Taken together, these two effects could lead to false rejection of the null hypothesis.

Third, the postoperative Glasgow Prognostic Score (poGPS) is determined solely by albumin and C-reactive protein (CRP) concentrations[2]. Determining statistical differences in poGPS at the same time as differences in CRP and albumin, at exactly the same cut-off values, artificially inflates the number of hypotheses being tested. In addition, no Bonferroni correction for multiple hypothesis testing was undertaken for the 15 *P* values given in *Table 3*; again, this could lead to a type I error and is an example of *P*-hacking.

We feel these points have led to Golder and colleagues overstating the likelihood of any treatment effect. Gut decontamination in colorectal surgery is an important issue that deserves a large high-quality RCT.

Disclosure

The authors declare no conflict of interest.

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1 Golder AM, Steele CW, Conn D, MacKay GJ, McMillan DC, Horgan P *et al.* Effect of preoperative oral antibiotics in combination with mechanical bowel preparation on inflammatory response and short-term outcomes following left-sided colonic and rectal resections. *BJS Open* 2019; **3**: 830–839.
2 Watt DG, McSorley ST, Park JH, Horgan PG, McMillan DC. A postoperative systemic inflammation score predicts short- and long-term outcomes in patients undergoing surgery for colorectal cancer. *Ann Surg Oncol* 2017; **24**: 1100–1109.

Authors' reply: Effect of preoperative oral antibiotics in combination with mechanical bowel preparation on inflammatory response and short-term outcomes following left-sided colonic and rectal resections

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We acknowledge Hartrick and colleagues for their interest in and comments regarding our study[1]. They correctly note that our study involved two longitudinal groups (control group before 2015 and test group after 2015). This was stated clearly in the Methods section and acknowledged in the limitations paragraph of the Discussion. This study was carried out after a change in routine clinical practice within our centre regarding the use of oral antibiotics and mechanical bowel preparation, and this potential limiting factor was therefore unavoidable. Despite this, both groups were from an entirely enhanced recovery after surgery era, which we hope would minimize other unmeasured variations in practice. Nonetheless, as with any similar form of study, we were unable to identify or account for all potential variables, hence our interest in ongoing RCTs within this field.

Hartrick *et al.* correctly note that a small proportion of patients in the test group had colorectal resection for benign disease, unlike the control group in which all resections were carried out for malignant disease. This was documented clearly in the Methods and Results sections, and also acknowledged in the limitations paragraph of the Discussion. For several reasons, we do not believe this introduced a significant bias to the results. The proportion of these patients was small (less than 15 per cent) and, although the authors have raised concerns regarding the possible heightened inflammatory state in malignant compared with benign disease, we propensity score-matched for the preoperative systemic inflammatory response (modified Glasgow Prognostic Score) with good balance between test and control groups (Cramer's V = 0.018). By convention, *P* values for significance are not usually presented after matching, as the very fact that those variables have been used to generate the propensity scores leads to inherent bias and renders inference illogical. For this reason, Cramer's V was calculated before and after matching (*Tables 1* and *2* respectively), along with a 'butterfly plot' of propensity score distribution. Both methods showed improvement in balance after matching.

The authors correctly state that the C-reactive protein and albumin cut-offs for days 3 and 4 were the same as those used to calculate the postoperative Glasgow Prognostic Score on days 3 and 4. The outcomes included in *Table 3* are largely related – both the postoperative inflammatory state on postoperative days 3 and 4 and the development of postoperative complications[2]. As a result, the likelihood of a type I error is substantially less than it would have